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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,824	08/08/2001	Dong-Mei Feng	20183YCA	7413

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EXAMINER

CHISM, BILLY D

ART UNIT	PAPER NUMBER
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1654

DATE MAILED: 07/15/2003

7

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/924,824

Applicant(s)

FENG, DONG-MEI

Examiner

B. Dell Chism

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 May 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 14-17 and 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 and 18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to Paper No. 6, filed 12 May 2003, wherein Applicant elected, with traverse, Group I claims 1-13 for examination. Also, Applicant cancelled claims 20-25 without prejudice to filing a divisional application. Claim 18 was excluded in the previous office action, wherein claim 18 was intended to be in Group I, claims 1-13 and 18. Thus, claims 1-13 and 18 are under consideration.

Applicant traverses the restriction requirement based on the fact that the Examiner did not provide examples of other methods for which the products could be used. The Examiner explained insofar as is required to establish possible "other methods" of use. Thus, this argument is not persuasive. Furthermore, as part of the obvious distinctness of the Groups I and II-III, a search for one group would not be coextensive with the other groups, and would pose and undue burden on the Examiner. For these reasons and those set forth in the previous office action, the Applicant's arguments are not persuasive and the restriction requirement is made FINAL.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 11 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a "written description" rejection, rather than an enablement rejection under 35

U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the "written description" inquiry, is *whatever is now claimed*" (see page 1117).

A review of the language of the claim indicates that these claims are drawn to a genus, i.e., cytotoxic-oligopeptide conjugate of a vinca alkaloid derivative that may be useful in the treatment of prostate cancer.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states "An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention".

There is a single set of species of the claimed genus disclosed that is within the scope of the claimed genus, i.e., vinca alkaloid derivatives. The disclosure of a single disclosed species

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may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claims encompass numerous species that are not further described and would not share structural description or similarity with the disclosed genus. There is substantial variability among the species encompassed by the wording of the claims. Applicant should limit the claimed invention to those compounds that are vinca alkaloid compositions.

One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus of which comprises all cytotoxic-oligopeptide conjugates. The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed” (see *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Claims 9-13 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is rejected for being indefinite for having two different sequences identified by SEQ ID NO: 82.

Claim 10 is indefinite wherein it is not clear by the formatting what is optional. The claim just states, “which is selected from” and there is no indication that the general structure remains the same and the changing component or the “selected from” aspect is the sequence structures.

Claim 11 is indefinite for the recitation of "compound of Claim 1" wherein there is no antecedent basis for the claimed "compound".

Claim 12 is indefinite for the recitation of "compound of Claim 5" wherein there is no antecedent basis for the claimed "compound".

Claim 18 is indefinite for the recitation of "compound of Claim 1" wherein there is no antecedent basis for the claimed "compound".

Claim 13 is rejected for depending from rejected claim 10.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-6, 11-12 and 18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3-5, 11-12 of U.S. Patent No. 5,866,679 (DeFeo-Jones *et al.*) and the teachings of Metzler in BIOCHEMISTRY page 370, 1977 (Displacement Reactions on Carbonyl Groups).

DeFeo-Jones *et al.* teach and claim a conjugate of formula II wherein: "oligopeptide is an oligopeptide that is specifically recognized by the free prostate specific antigen (PSA) and is capable of being proteolytically cleaved by enzymatic activity of free prostate specific antigen". The XL in the DeFeo-Jones *et al.* may be absent, an amino acid or a diamine. In case XL contains an amine the carboxyl terminus of the oligopeptide and the amine group of the linker form an amide link as show in claim 5 (top structure). See entire document.

However, DeFeo-Jones *et al.* do not teach the presence of OH bond in the linker or the use of an ester linkage in the conjugate for achieving the claimed activity.

The secondary reference discloses that under physiological conditions amides and esters (thioesters) undergo a displacement reaction wherein the displacement on carbonyl group occurs.

A person of ordinary skill in the art at the time of the invention would have expected that the use of a hydroxy containing linker attached to the cytotoxic agent would facilitate the formation of an ester linkage in the conjugate and the resulting conjugate would be expected to undergo displacement under physiological conditions much like having an amide linkage. See page 370 of BIOCHEMISTRY. The use of a hydroxy or an amine containing linker is a matter of choice; either entity would eventually take part in the process of transacylation for exhibiting bioactivity.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1-6, 11-12 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by DeFeo-Jones *et al.* DeFeo-Jones *et al.* (claims 11-13, column 170 lines 37-column 171 lines 22) teach a conjugate of present claims 1-6, 11-12 and 18.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

8. Claims 1, 3-4, 7 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Garsky *et al.* (US 5,948,750).

Garsky *et al.* discloses conjugates useful in treating prostate cancer comprising a cytotoxic agent (vinblastine and desacetyvinblastine, claim 4), attached to the C-terminus of the oligopeptide (col. 23 and col. 27, lines 31-34). The oligopeptide sequence of the amino acids are selectively proteolytically cleaved by the free PSA and wherein the means of attachment is through a sterically hindered hydroxy alkyl amino chemical linker by an ester bond comprising hydroxy moiety of the chemical linker, which comprises the presently claimed motifs, e.g., TyrGln/SerSer(leu,Nle), etc, and a blocking group (col. 3-7). Additionally, the presence of a cyclic amino acid having a hydrophilic substituent as part of the oligopeptides, contributes to the aqueous solubility of the conjugate (col. 3, lines 1-10). A person of ordinary skill in the art at the

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time of the invention would have immediately envisaged the instant claims in view of the teachings of the applied reference; hence the claims are anticipated by the art.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Conclusions

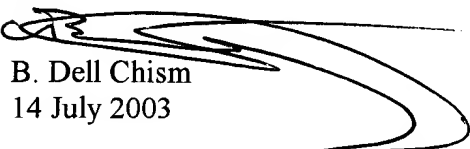
No claims are allowed. Claim 8 is objected to for depending from rejected claim 5.

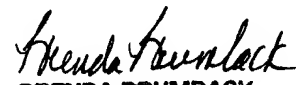
Any inquiry concerning this communication or earlier communications from the examiner should be directed to B. Dell Chism whose telephone number is 703-306-5815. The examiner can normally be reached on 7:30 AM - 4:30 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 703-306-3220. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

B. Dell Chism
14 July 2003




BRENDA BRUMBACK
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